"The Spermatogenesis of an Hemipteron, Euschistus," Thos. H. Montgomery, Jr.

"The Life History of the *Scolex polymorphus* of the Woods Hole Region," Winterton C. Curtis.

SPECIAL ARTICLES

ON SOME CONDITIONS OF TISSUE GROWTH, ESPECIALLY IN CULTURE MEDIA

IN a paper on the regeneration of epithelium published almost fourteen years ago[1] I analyzed some of the internal and external factors in the growth of mammalian tissues and demonstrated the existence of stereotropism in regenerating epithelial cells. I also cited certain statements of other observers which suggested to me the existence of a stereotropic sensitiveness in other varieties of growing vertebrate tissues.

At that time I furthermore had the opportunity to observe that epithelium might grow and show its stereotropic reaction without relation to the underlying tissue, growing merely in contact with blood coagula. This observation suggested to me the possibility of cultivating tissues of vertebrates in culture media *in vivo* as well as *in vitro,* in a similar manner as bacteria had been cultivated. My previous observations on the importance of the contact with solid substances in tissue growth induced me to use solid coagula as the culture medium.[2] I published a communication concerning these first experiments (which had been carried out in Baltimore).[3] In further experiments accidental conditions made it necessary to study the growth of mammalian tissues in culture media with the animal body acting as an incubator. The results of these experiments have been published in detail.[4] To our knowledge in these earlier experiments, for the first time the attempt was recorded in the literature to grow tissues of higher animals under artificial conditions, to separate through culture media experimentally growing epithelial from connective tissue cells and furthermore to study the influence of the addition of certain chemicals upon the growth of tissues.[5]

Demands of other investigations prevented me from extending these experiments into various directions, as I had planned to do for a considerable number of years. Only recently I resumed these studies and I analyzed further the growth of tissues in solid coagula, especially differentiating between the reactions of stroma and parenchyma in tissue growth in culture media. Here I will add the results of some further studies which were made in conjunction with my collaborator, Dr. Moyer S. Fleisher, and a more detailed account of which will appear elsewhere.

1. We investigated to what extent oxygen is necessary for the growth of mammalian tissues in culture media, a problem which had interested me from the beginning of my experiments. In the case of certain higher plants it has been recently shown that a limited anaerobic growth is possible. We used various methods of anaerobic culture methods and we also studied the effect of a diminution in the supply of oxygen. Our results show that growth ceases if oxygen is lacking or noticeably diminished. This applies to various tissues. A noteworthy difference in the reaction of various tissues to lack of oxygen we could not observe. Under these conditions tissues not only cease to grow, but they die. It is much more difficult to determine the effect of an increase in the tension of oxygen on tissue growth. Our experiments, however, make it very probable that in certain cases the life and growth of tissues is favorably influenced if pure oxygen takes the place of air surrounding the culture media.

2. We studied the effect of the combined growth of an oidium-like organism[6] and of

[1] "Ueber Regeneration des Epithels" (chapter 13), *Archiv f. Entw'mech.,* Bd. VI., 1898.

[2] I referred to this circumstance again in a communication to the Society of Experimental Biology and Medicine, Proceedings of the 44th meeting, May 17, 1911.

[3] Chicago, 1907.

[4] *Archiv f. Entw'mech.,* Bd. XIII., 1902; *Journ. Med. Research,* Vol. VIII., 1902; *Journ. Am. Med. Association,* 1901.

[5] *Zeitschrift f. Krebsforschung,* Bd. V., 1907.

[6] This organism was studied in conjunction with Dr. George J. Moore, of St. Louis, and will be described elsewhere.

kidney tissue. This organism had been injected into the circulation of a rabbit and at various periods after the injection pieces of the kidney were transferred into the culture media. In these experiments we found not only that both kidney tissue, stroma and parenchyma, and organism may grow side by side in the culture media, but that under certain conditions the growth of the kidney cells may be quantitatively increased.

It will be of interest to extend these studies to other well-defined microorganisms and to test the effect of their metabolic products and direct action on tissue growth.

3. The stereotropic sensitiveness of connective tissue cells can very well be observed in the process of atresia of the ovarian follicle. At a period when the degeneration of the granulosa has set in, connective tissue cells begin to grow from the surrounding theca into the follicular cavity and to fill it more or less completely. Here we can notice that usually the connective tissue cells do not grow directly into the cavity but move in contact with the wall of the follicle, thus forming a peripheral layer of connective tissue which gradually enlarges as more cells are added.

In certain cases, however, we may observe that connective tissue cells grow directly into the cavity. In these cases it is probable that the viscosity of the follicular fluid is relatively great and that a viscous fluid may permit a direct ingrowth of some tissue cells.

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ON AN INTERPOLATION FORMULA USED IN CALCULATING TEMPERATURE COEFFICIENTS FOR VELOCITY OF VITAL ACTIVITIES, TOGETHER WITH A NOTE ON THE VELOCITY OF NERVE CONDUCTION IN MAN

INQUIRIES, both written and verbal, have come to me asking for information concerning a formula which has been employed in some of my physiological papers on temperature coefficients.

In this communication I wish to answer these inquiries (1) by referring to the antecedents and mathematical significance of the formula as briefly as I may, and (2) by giving one or two examples of its application.

In the first place it must be stated that the formula in question, so far as my work is concerned, is entirely an empirical one. Wherever a series of quantities varies with some exponential factor the formula has been found to be fairly satisfactory for extra- and interpolation. Its origin, as far as I (who am not a mathematician) know, is probably "lost in antiquity." Professor Max Bodenstein, of Hanover, has told me, however, that he thought Berthelot first used it in chemistry. Just lately I find that Bodenstein[1] himself made use of the formula in 1899 for the determination of the temperature coefficient of chemical reaction velocities.

On the other hand, the formula of van't Hoff[2] and Arrhenius,[3] among others, were developed from thermodynamic considerations and therefore have important theoretical foundations.

However, the formula I use,

$$\left(\frac{k_1}{k_0}\right)^{\frac{10}{t_1-t_0}} = Q_{10} \qquad (1)$$

is practically the same, I find, as one of van't Hoff's,[4] namely,

$$\log_{10} k = a + bt. \qquad (2)$$

For if the values of k in (2) for two different temperatures are known, then this equation may be derived:

$$\frac{k_{t+10}}{k_t} = 10^{10 \cdot b}. \qquad (3)$$

Equation (1) is probably more convenient for the calculation of quotients for intervals of 10 degrees (temperature coefficients), but it is also more cumbersome for the calculation

[1] Bodenstein, M., *Zeitschrift für physikalische Chemie*, 1899, Bd. 29, S. 332.

[2] Van't Hoff, "Etudes de dynamique chimique," 1884, p. 115.

[3] Arrhenius, *Zeitschrift für physikalische Chemie*, 1899, Bd. 4, S. 226; "Immunochemie," Leipzig, 1907.

[4] Van't Hoff, *Vorlesungen über theoretische und physikalische Chemie*, 1898, I., S. 224.